

CONTINUOUS EXTRACTION STRATEGIES FOR MONOCLONAL ANTIBODIES: FROM MACRO- TO MICRO-SCALE

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Aqueous two-phase extraction (ATPE) have shown to be a valuable option for the downstream processing of biopharmaceuticals, combining a high biocompatibility and selectivity with an easy and reliable scale up. Moreover, ATPE can overcome some of the technical drawbacks currently encountered using established purification platforms, such as batch operation, diffusional limitations and scale-related problems. We have developed a continuous ATPE process incorporating three different steps (extraction, back-extraction and washing) for the capture of monoclonal antibodies (mAbs). The ATPE process was set up and validated in a pump mixer-settler battery and successfully applied to a Chinese hamster ovary and a PER.C6® cell supernatant.

The limited predictive design of ATPE, however, has restrict its applicability to current downstream processing. Microscale process techniques have recently emerged as effective tools for expediting bioprocess design in a cost-effective manner. ATPE in a microfluidic platform was therefore designed and tested for mAbs extraction, as an effective tool to accelerate bioprocess design and optimization. Furthermore, this platform has the potential of combining the process efficiency of ATPS with the reduced times and volumes associated with microfluidics, as well as the possibility to multiplex and parallel process in real downstream processes. In this way, we have develop a microfluidic channel-based toolbox for the rapid screening of antibody extraction conditions. Several microfluidic structures have been designed including a multiplexed structure that allows a simple negative-pressure driven rapid screening of up to 8 continuous extraction conditions simultaneously, using less than 20 μL of each phase forming solution per experiment. Results obtained from this device can be further applied in a second microfluidic structure (Figure 1) that integrates multiple-step continuous extraction protocols.